

CLAIMS

What is claimed is:

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1. A monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain, wherein the antibody or antigen binding fragment does not crossreact with digoxin.

2. The monoclonal antibody of Claim 1 selected from the group consisting of: 1-10, 5A12, 7-1, 8E4 and an antigen binding fragment thereof.

3. The monoclonal antibody of Claim 1 which has a binding affinity constant for ouabain of at least about $2 \times 10^{-8}M$.

10 4. The monoclonal antibody of Claim 1 which has a binding affinity constant for ouabain of at least about $3 \pm 1 \times 10^{-7}M$.

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5. A monoclonal antibody or antigen binding fragment thereof having the same binding specificity as a monoclonal antibody selected from the group consisting of: 1-10, 5A12, 7-1 and 8E4.

15 6. A hybridoma cell line which produces a monoclonal antibody selected from the group consisting of: 1-10, 5A12, 7-1, 8E4, a monoclonal antibody having the same binding specificity as 1-10, 5A12, 7-1 or 8E4, and an antigen binding fragment thereof.

7. A method of making a monoclonal antibody or antigen binding fragment thereof having a particular binding specificity for a hapten, comprising the steps of:
- a) immunizing a mammal with the hapten bound to an antibody which does not have the particular binding specificity for the hapten and which was produced by the mammal;
 - b) fusing splenocytes of the mammal with immortalized cells to produce hybridomas;
 - c) selecting from the hybridomas a hybridoma which produces a monoclonal antibody or antigen binding fragment thereof having the particular binding specificity for the hapten.

8. A method of making a monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain and which does not crossreact with digoxin, comprising the steps of:
- a) immunizing a mammal with ouabain bound to an antibody which has binding specificity for a glycoside;
 - b) fusing splenocytes of the mammal with immortalized cells to produce hybridomas;
 - c) selecting from the hybridomas a hybridoma which produces a monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain and which does not crossreact with digoxin.

9. The method of Claim 8 wherein the monoclonal antibody is selected from the group consisting of: 1-10, 5A12, 7-1, 8E4 and an antigen binding fragment thereof.
10. The method of Claim 8 wherein ouabain is covalently bound to the antibody 26-10.
11. The method of Claim 8 wherein the mammal is a mouse.

12. A method for identifying ouabain or a ouabain-like compound in a mammal comprising the steps of:
- a) obtaining a sample from the mammal;
 - b) contacting the sample with a monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain, wherein the antibody or antigen binding fragment does not crossreact with digoxin, under conditions in which an immunocomplex between the antibody or antigen binding fragment thereof and ouabain or the ouabain-like molecule can occur, whereby the presence of ouabain or ouabain-like compound can be identified by identifying the presence of the immunocomplex.
13. The method of Claim 12 wherein the sample from the mammal is selected from the group consisting of: plasma, serum and urine.
14. The method of Claim 12 wherein the monoclonal antibody is selected from the group consisting of: 1-10, 5A12, 7-1, 8E4 and an antigen binding fragment thereof.
15. A method for monitoring ouabain-like compound or digitoxin in a mammal comprising the steps of:
- a) obtaining samples over a period of time from the mammal;
 - b) contacting each sample with a monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain, wherein the antibody or antigen binding fragment does not crossreact with digoxin, under conditions in which an immunocomplex between the antibody or antigen binding fragment thereof and the ouabain-like compound or the digitoxin can occur, thereby monitoring ouabain-like compound or digitoxin in the mammal.

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21. A method of diagnosing the presence of ouabain- or ouabain-like compound-associated congestive heart failure in a mammal comprising the steps of:
 - a) obtaining a sample from the mammal;
 - b) contacting the sample with a monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain, wherein the antibody or antigen binding fragment does not crossreact with digoxin, under conditions in which an immunocomplex between the antibody or antigen binding fragment thereof and ouabain or a ouabain-like molecule can occur, thereby producing a test sample; and
 - c) determining whether formation of the immunocomplex in the test sample occurs; and
 - d) comparing the immunocomplex formation of c) to immunocomplex formation in a control sample,wherein if the immunocomplex formation in the test sample is altered compared to the immunocomplex formation in the control sample, then ouabain- or ouabain-like compound-associated congestive heart failure is present in the mammal.
22. The method of Claim 21 wherein the sample from the mammal is selected from the group consisting of: plasma, serum and urine.
23. The method of Claim 21 wherein the monoclonal antibody is selected from the group consisting of: 1-10, 5A12, 7-1, 8E4 and an antigen binding fragment thereof.
24. A method of diagnosing the presence of ouabain- or ouabain-like compound-associated cardiomyopathy in a mammal comprising the steps of:
 - a) obtaining a sample from the mammal;

- b) contacting the sample with a monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain, wherein the antibody or antigen binding fragment does not crossreact with digoxin, under conditions in which an immunocomplex between the antibody or antigen binding fragment thereof and ouabain or a ouabain-like molecule can occur, thereby producing a test sample; and
- c) determining whether formation of the immunocomplex in the test sample occurs; and
- d) comparing the immunocomplex formation of c) to immunocomplex formation in a control sample,
- wherein if the immunocomplex formation in the test sample is altered compared to the immunocomplex formation in the control sample, then ouabain- or ouabain-like compound-associated cardiomyopathy is present in the mammal.

25. The method of Claim 24 wherein the sample from the mammal is selected from the group consisting of: plasma, serum and urine.

26. The method of Claim 24 wherein the monoclonal antibody is selected from the group consisting of: 1-10, 5A12, 7-1, 8E4 and an antigen binding fragment thereof.

27. A method of diagnosing the presence of ouabain- or ouabain-like compound-associated renal failure in a mammal comprising the steps of:

- a) obtaining a sample from the mammal;
- b) contacting the sample with a monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain, wherein the antibody or antigen binding fragment does not crossreact with digoxin, under conditions in which an immunocomplex between the antibody or antigen

c) determining whether formation of the immunocomplex in the test sample occurs; and

wherein if the immunocomplex formation in the test sample is greater than the immunocomplex formation in the control sample, then ouabain- or ouabain-like compound-associated renal failure is present in the mammal.

29. The method of Claim 27 wherein the monoclonal antibody is selected from the group consisting of: 1-10, 5A12, 7-1, 8E4 and an antigen binding fragment thereof.

30. A method of diagnosing the presence of ouabain- or ouabain-like compound-associated salt sensitivity in a mammal comprising the steps of:

- obtaining a sample from the mammal;
- contacting the sample with a monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain, wherein the antibody or antigen binding fragment does not crossreact with digoxin, under conditions in which an immunocomplex between the antibody or antigen binding fragment thereof and ouabain or a ouabain-like molecule can occur, thereby producing a test sample; and
- determining whether formation of the immunocomplex in the test sample occurs; and

d) comparing the immunocomplex formation of c) to immunocomplex formation in a control sample, wherein if the immunocomplex formation in the test sample is greater than the immunocomplex formation in the control sample, then ouabain- or ouabain-like compound-associated salt sensitivity is present in the mammal.

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31. The method of Claim 30 wherein the sample from the mammal is selected from the group consisting of: plasma, serum and urine.

32. The method of Claim 30 wherein the monoclonal antibody is selected from the group consisting of: 1-10, 5A12, 7-1, 8E4 and an antigen binding fragment thereof.

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~~33.~~ A method of treating cardiac glycoside toxicity in a mammal comprising administering to the mammal a therapeutically effective amount of a monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain, wherein the antibody or antigen binding fragment does not crossreact with digoxin.

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34. The method of Claim 33 wherein the monoclonal antibody is selected from the group consisting of: 1-10, 5A12, 7-1, 8E4 and an antigen binding fragment thereof.

35. The method of Claim 33 wherein the cardiac glycoside is selected from the group consisting of: ouabain and digitoxin.

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~~36.~~ A method of treating hypertension in a mammal comprising administering to the mammal a therapeutically effective amount of a monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain, wherein the antibody or antigen binding fragment does not crossreact with digoxin.

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37. The method of Claim 36 wherein the monoclonal antibody is selected from the group consisting of: 1-10, 5A12, 7-1, 8E4 and an antigen binding fragment thereof.

38. A pharmaceutical composition comprising a monoclonal antibody or antigen binding fragment thereof having binding specificity for ouabain, wherein the antibody or antigen binding fragment does not crossreact with digoxin, and a pharmaceutical acceptable carrier.

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